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33. (New) The method of Claim 28, wherein the plants are dicotyledonous plants or monocotyledonous plants and wherein the plant tissues or plant cells are derived from dicotyledonous plants or monocotyledonous plants.
34. (New) The method of Claim 28, wherein the plants are dicotyledonous plants and wherein the plant tissues or plant cells are derived from dicotyledonous plants.
35. (New) The method of Claim 33, wherein the plants are tobacco plants.
36. (New) The method of Claim 28, wherein the plants are monocotyledonous plants and wherein the plant tissues or plant cells are derived from monocotyledonous plants
37. (New) The method of Claim 35, wherein the plants are cereal plants.

#### REMARKS

These remarks are in response to the Office Action mailed September 5, 2002. Claims 10-27 were previously pending in the present application. Entry of new claims 28-37 is respectfully requested. Claims 10-27 have been cancelled without prejudice. Applicants maintain the right to prosecute the cancelled claims in any related application claiming the benefit of priority of the subject application. Therefore, Claims 28-37 are currently pending.

Support for Claims 28-37 is found throughout the specification and in particular, in the substitute specification on page 2 at line 36 to page 3 at line 22, on page 5 lines 31-32, on page 7 at lines 15-22, on page 8 at line 3 to page 14 line 15. Applicants submit that Claims 28-37 place the present application in condition for allowance.

A substitute specification is submitted as required by the Examiner under 37 CFR 1.125(a). The substitute specification corrects informalities objected to by the Examiner and does not add new matter. Entry of the substitute specification is requested.

Corrected drawings as required by the Examiner are submitted herewith. The corrected drawings address informalities objected to by the Examiner for reasons indicated on the form PTO 948 accompanying the Office Action mailed September 5, 2002. The corrected drawings contain no new matter. Entry of corrected drawings is requested.

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Regarding Amendments the Specification

In the Official Action mailed September 5, 2002, the Examiner stated that amendments to the specification filed July 9, 2002, were not entered because no marked-up copy of the paragraphs was submitted. Although Applicants disagree and are prepared to submit evidence that marked-up copies of the paragraphs were submitted with the amendment filed July 9, 2002, Applicants suggest that the substitute specification submitted herewith renders this question moot. The amendments Applicants requested in the Amendment filed 9 July, 2002, were also required by the Examiner in the Official Action mailed September 5, 2002. Thus, the substitute specification filed under 37 CFR §1.125(a) submitted herewith as required by the Examiner contains the amendments to the specification that Applicants previously requested to be entered.

Regarding Compliance with Sequence Rules

The Examiner further stated that the application fails to comply with the requirements of 37 CFR §1.821 through §1.825, noting that sequence identifiers are missing from the specification on page 8, line 15, page 9, line 15, and page 10, third line from the bottom. The substitute specification filed under 37 CFR §1.125(a) submitted herewith includes the sequence identifiers required by the Examiner. Applicants submit that the substitute specification submitted herewith places the application in compliance with the requirements of 37 CFR §1.821 through §1.825.

Regarding the Substitute Specification

In the Official Action mailed September 5, 2002, the Examiner objected to informalities in the specification and required a substitute specification excluding claims under 37 CFR §1.125(a). In response, Applicants submit a substitute specification under 37 CFR §1.125(a) and request that the substitute specification be entered into the record. In addition, Applicants enclose a clean copy of the original specification excluding claims for the Examiner's inspection..

Changes found in the substitute specification in response to the Examiner's requirements are as follows:

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1. The Examiner noted that sequence identifiers were missing from the original specification on page 8 at line 5, page 9 at line 15, and page 10 at third line from the bottom. (Official Action, Section 3.) Applicants have added sequence identifiers as required by the Examiner, on page 9 at line 16, page 10 at line 13, and page 10, line 27 of the substitute specification. In addition, a sequence identifier for SEQ ID NOS: 2 & 3 has been added at page 3 at line 30, in compliance with 37 CFR §1.821(d).

2. The Examiner objected to footnotes on pages 1 and 4 of the original specification, indicating translator's notes, and required clarification and correction. (Official Action Section 4.a.) Translator's notes have been removed. The page number mentioned in translator's note on page 1 of the original specification has been corrected on page 1 at line 28 of the substitute specification. The correction suggested in the translator's note on page 4 of the original specification has been made in the substitute specification on page 5 at line 21.

3. The Examiner objected to lack of section headings and location of description of the drawings. (Official Action Section 4.b.) Section headings have been added and are found in the substitute specification on page 1 at line 4, page 1 at line 13, page 2 at line 31, page 3 at line 23, and on page 4 at line 21. The description of the drawings has been moved from page 9 at line 19 to page 10 at line 20 in the original specification to page 3 at line 24 to page 4 at line 20 in the substitute specification, located after the Summary of the Invention section and before the Detailed Description of the Invention section.

4. The Examiner objected to letter quality. (Official Action Section 4.c.) A substitute specification with good letter quality is submitted herewith. In addition, a copy of the original specification with good letter quality is submitted herewith for the Examiner's inspection.

5. In addition, eight (8) single letter changes to correct spelling have been made in the substitute specification. These changes do not introduce new matter, and were made solely to correct spelling. These corrections are:

- page 6 at line 4, correct dicotyledonuous to read "dicotyledonous"
- page 6 at line 32, correct dicotyledonuous to read "dicotyledonous"
- page 9 at line 23, correct Phytophthora to read "Phytophthora"

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- page 9 at line 32, correct plasmadesmata to read "plasmodesmata"
- page 10 at line 19, correct Phytophtora to read "Phytophthora"
- page 10 at line 26, correct hydrphilic to read "hydrophilic"
- page 14 at line 14, correct Phytophtora to read "Phytophthora"
- page 15 at line 2, correct irrigatin to read "irrigation"

If the Examiner determines that these changes are not acceptable in a substitute specification filed under 37 CFR § 1.125(a), then Applicants will submit a substitute specification under 37 CFR § 1.125(b).

Regarding Objections to the Drawings

In the Official Action mailed September 5, 2002, drawings were objected to for reasons indicated on accompanying form PTO 948. The Examiner required corrected drawings to be submitted (Official Action Section 5.) Applicants herewith submit corrected drawings for Figures 1 to 8, and request that objections to the drawings be withdrawn.

Regarding Claim Rejections

In the Official Action mailed September 5, 2002, Claims 10-27 were rejected. Applicants have cancelled Claims 10-27 without prejudice and have added new Claims 28-37. Because Claims 10-27 have been cancelled, these claim rejections have been rendered moot. Nonetheless, Applicants respectfully address the Examiner's rejections in remarks presented below.

Rejections Under 35 U.S.C. §112, First Paragraph, Enablement

The Examiner rejected Claims 10-27 under 35 USC § 112, first paragraph, on grounds that the specification, while being enabling for a method of producing potato plants having tolerance to drought, fungal infection and salt by transformation with a nucleic acid encoding the pr17 protein operably linked to an N-terminal extension having the sequence of SEQ ID NO: 1, allegedly does not reasonably provide enablement for: a) a method of producing plants that are tolerant of temperature extremes by transformation with a nucleic acid encoding the pr17 protein or other derivatives of pr17; or b) a method of producing plants that are tolerant of temperature

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extremes by transformation with that nucleic acid or other derivatives of pr17 or a method of using a multitude of DNA molecules that encode a protein with "an intrinsic affinity to plasmodesmata" to produce any and all plant species that are tolerant of drought, fungal infection, salt and temperature.

Claims 10-27 have been cancelled, rendering this rejection moot. Nonetheless, Applicants wish to point out that support for claims reciting increased tolerance to extreme temperature is found in the substitute specification on page 3 at lines 8-10, stating that the invention relates "to the production of plants or parts thereof having an increased tolerance against drought and/or fungal infections and/or increased salt concentrations and/or extreme temperatures, i.e. cold and/or heat."

The Examiner notes that the specification provides guidance for production of a vector encoding the pr17 protein operably linked to an N-terminal extension of SEQ ID NO: 1, but allegedly fails to provide guidance for isolation or synthesis of nucleic acids encoding other derivatives of pr17 or proteins with "an intrinsic affinity to plasmodesmata" or for using those nucleic acids to produce plants that are tolerant of drought, fungal infection, salt and temperature.

Applicants point out that claims reciting proteins with "an intrinsic affinity to plasmodesmata" have been cancelled. In addition, as long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement of 35 USC§112 is satisfied. (MPEP §2164.01(b)).

Further, the Examiner notes that not all plants are susceptible to infection by *Phytophthora infestans*, and argues that it allegedly is unclear how transformation with any protein could increase the tolerance of a plant to infection by *Phytophthora infestans* or how such an increase could be measured in such plants.

A specification must enable those skilled in the art to practice the claimed invention with undue experimentation. (MPEP §2164.05). Here, one of skill in the art would know that *only* those plants that are susceptible to infection by *Phytophthora infestans* would show increased tolerance to such an infection. Likewise, one of skill in the art would know that plants that are

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not susceptible to infection by *Phytophthora infestans* would not show increased tolerance to infection because infection never occurs. Measuring increased tolerance to infection by *Phytophthora infestans* in a susceptible transgenic plant produced by the claimed method is disclosed in Examples 4 and 6, and illustrated in Figures 5 and 6. In these Examples, leaf disks of transgenic and wild-type potato plants were inoculated with known spore concentrations of *P. infestans* and incubated under conditions that allow infectious zoospores to hatch (page 12 at lines 1-13; page 13 at lines 10-15) and at defined times after inoculation, infestation (bonitation) quantitatively assessed (page 12 at lines 13-15; page 13 at lines 14-15). Thus, the specification adequately enables claims reciting increased tolerance to infection by *Phytophthora infestans* to satisfy the requirement of 35 USC §112, first paragraph.

At Section 7, page 6, the Examiner notes that, given the specificity of protein-protein interactions and given that potato leaf roll virus does not infect all plants, it allegedly is unclear that a nucleic acid encoding pr17 + SEQ ID NO: 1 would work in other plants, particular distantly related ones like cereals. Here, the specification teaches how to carry out the methods of the present invention using *any* plant, monocotyledonous or dicotyledonous, without undue experimentation (see, page 5 at line 28 to page 6 at line 33, in particular page 6 at lines 31-33).

The proper test for enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. (MPEP §2164.01). Here, the specification teaches multiple transformation systems used successfully for various cereals (page 6 at lines 5-33), teaches how to identify transformed plant cells, plant tissues, and plants (page 6 at line 34 to page 7 at line 14), and teaches how to identify transgenic plants having increased tolerance as claimed (Example 3, 4, 5, 6, 7) using the potato leaf roll virus (PLRV) as a model system for a virus-encoded transport protein (page 8 at lines 3-7). Thus, the specification teaches how to practice the claimed invention using any plant.

In addition, one of skill in the art would know that luteoviruses such as PLRV can infect dicotyledonous plants and monocotyledonous plants, since pr17 of PLRV is analogous to movement protein of barley yellow dwarf luteovirus, as disclosed by Tacke *et al.* (1996, *Nature Biotechnology* 14:15971601, at page 1597, right column, second paragraph). Documents cited in the specification, the contents of which are incorporated by reference (see, page 1 at lines 14-16)

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illustrate the state of the art. (MPEP 608.01(p)). Thus, one of skill in the art would know that PLRV is an appropriate model system, since PLRV belongs to the luteoviruses that infect both dicotyledonous and monocotyledonous plants.

Rejections Under 35 U.S.C. §112, First Paragraph, Written Description

The Examiner rejected Claims 10-15 and 17-27 under 35 USC § 112, first paragraph, on the grounds that the claims are broadly drawn to a method of using a multitude of DNA molecules that encode a protein with an intrinsic affinity to plasmodesmata, while the specification describes a coding sequence from potato leaf roll virus that encodes pr17 with an N-terminal extension of SEQ ID NO: 1 and allegedly does not describe other DNA molecules encompassed by the claims, and the structural features that distinguish all such nucleic acids from other nucleic acids are not provided. Applicants note that claims reciting a protein with "an affinity to plasmodesmata" have been cancelled, rendering this rejection moot.

In addition, Applicants point out that structural and physical characteristics of pr17 are disclosed on page 8 at lines 7-21 of the specification, which describes an aminoterminal domain for homopolymer formation, a carboxyterminal domain for binding single-stranded amino acids, and plasmodesmatal localization of infection-derived and transgenic pr17 in phloem cells. The specification further discloses that expression of WT and mutated PLRV-TPs confers broad-spectrum resistance to viruses and increases in intracellular sugar and starch concentrations (page 8 at lines 21-27). Thus, the specification describes the distinguishing structural features of the claimed nucleic acids and the DNA molecules encompassed by the claims.

Rejections Under 35 U.S.C. §112, Second Paragraph

At Section 10, pages 8-10, Claims 10-27 were rejected under 35 USC § 112, second paragraph, as allegedly being indefinite. In particular, the Examiner stated that Claims 10 and 11 are indefinite in their recitation of "transfecting" and "transfected", respectively, and Claim 10 is indefinite in its recitation of "intrinsic affinity to plasmodesmata." Claims 10-27 have been cancelled herein without prejudice, rendering these rejections moot.

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The Examiner stated that the term "increased" in Claims 10, 18, and 23-27 is considered a relative term that renders the claims indefinite. Although Claims 10, 18, and 23-27 have been cancelled, rendering this rejection moot, Applicants point out that the term is defined in the specification in each context wherein the term is used. The term "increased" in "increased salt concentration" is defined as referring to the salt concentration in the soil leading to an increased ionic concentration in the plant which in turn leads to reduced growth (page 4 at lines 22-23). The specification further teaches that absolute concentrations, to be regarded as "increased," are different for different plants and can be determined by a skilled person according to standard methods (page 4 at lines 22-26). Example 7 discloses a range of defined salt (NaCl) concentrations used to define the tolerance of non-transgenic and transgenic lines of the potato variety "Linda." The term "increased" in "increased tolerance against drought" would be understood by one of skill in the art by reading the specification. For example, Example 5, Table 1, Figure 3, and Figure 4 disclose that the survival rate of transgenic plants is higher than the survival rate of wild-type (untransformed) plants under drought conditions. The term "increased" in "increased tolerance against fungal infections" would be understood by one of skill in the art by reading the specification. For example as disclosed in Examples 4 and 6 and illustrated in Figures 5 and 6, four transgenic lines (L4, L6, L7, L8) expressing pr17 showed significantly increased tolerance to infection by *Phytophthora infestans* compared with the nontransgenic wild-type line ("Linda"). Thus, the specification provides measurements of transgenic wild-type plants as a "known standard" for determining the meaning of the term "increase" with respect to measurements of transgenic plants produced in accordance with the claimed methods. Accordingly, the term "increased" would be understood by a skilled artisan.

The Examiner stated that the term "extreme" in Claim 10 is a relative term that allegedly renders the claim indefinite. Claim 10 has been cancelled without prejudice, rendering this rejection moot. Applicants point out that the term is defined in the specification in each context wherein the term is used. The term "extreme temperatures" is presented as an example of a stress factor of an abiotic nature (page 1 at lines 19-20) and it is noted that "drought, heat or salinity of the soil restrict the possibility of cultivating crop plants" in stress-dominated habitats (page 1 at lines 21-22) and agriculture suffers heavy loss through abiotic stress (page 1 a line 23).



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The term "extreme" as in "extreme temperatures" is additionally clarified by phrase "i.e. cold and/or heat" (page 3 at line 10). Thus, the specification teaches that term "extreme" in the phrase "extreme temperature" is a type of abiotic stress, and stress restricts cultivation or causes loss of crop plants, and stress responses of plants can be measured as discussed above. Accordingly, the term "extreme" would be understood by a skilled artisan.

Applicants have cancelled rejected Claims 10-27 and respectfully submit that new Claims 28-37 satisfy the requirements of 35 USC § 112, second paragraph, and entry of these new claims places the present application in condition for allowance.

Rejections Under 35 U.S.C. §102

In the Official Action mailed September 5, 2002, the Examiner rejected Claims 10-27 under 35 USC § 102(b) as allegedly anticipated by Tacke *et al.* (1996, *Nature Biotechnology* 14:1597-1601) and by Herbers *et al.* (1997, *The Plant Journal* 12:1045-1056) taken with the evidence of Tacke *et al.* (*supra*). Claims 10-14, 17-19, 23 and 27 were rejected under 35 USC § 102(b) as allegedly anticipated by Lucas (WO 97/06669). Claims 10-27 have been cancelled without prejudice, thereby rendering these objections moot. Applicants submit that entry of new Claims 28-37 would place the present in condition for allowance. Nonetheless, Applicants would like to discuss the cited references below.

Tacke *et al.*, allegedly describe, *inter alia*, a method of producing transgenic potato plants transformed with a nucleic acid encoding PLRV pr17 with and without a hydrophilic N-terminal extension of SEQ ID NO: 1. The Examiner proposed that this method would inherently be a method of increasing tolerance of drought, fungal infection, salt and temperature, as the method steps are identical to the instantly claimed method. Herbers *et al.* allegedly describe, *inter alia*, a method of producing tobacco plants transformed with a nucleic acid encoding the potato leaf roll virus (PLRV) movement protein MP 17 with the N-terminal extension taught by Tacke *et al.* *supra*. The Examiner proposed that because these plants are notably shorter than control plants, they would have increased tolerance to drought due to lower surface area. Lucas (WO 97/06669) allegedly describes, *inter alia*, a method of producing tobacco plants by transformation with the movement protein of tobacco mosaic virus. The Examiner proposed that because the

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transformed plants have increased dark respiration under high temperatures and are notably shorter, the plants are heat tolerant and have increased tolerance to drought.

Neither Tacke *et al.* nor Herbers *et al.* nor Lucas teach or suggest a method for production of plants with increased tolerance against drought, fungal infection, increased salt concentration, or extreme temperatures. In addition, neither Tacke *et al.* nor Herbers *et al.* nor Lucas teach or suggest testing regenerated transgenic plants to identify those transgenic plants transformed with a nucleic acid which encodes a virus-encoded transport protein that has increased tolerance against drought, fungal infections, increased salt concentrations or extreme temperature while showing essentially normal growth. Furthermore, neither Tacke *et al.* nor Herbers *et al.* nor Lucas teach or suggest using transgenic plants identified as having increased tolerance to produce at least one transgenic plant line, plant, plant part, or plant cell having increased tolerance against drought, fungal infections, increased salt concentrations or extreme temperature and showing essentially normal growth. Accordingly, these references would not have anticipated the claimed invention.

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### CONCLUSION

In summary, for the reasons set forth herein, Applicants maintain that new Claims 28-37 clearly and patentably define the invention, respectfully request allowance of the claims now pending.

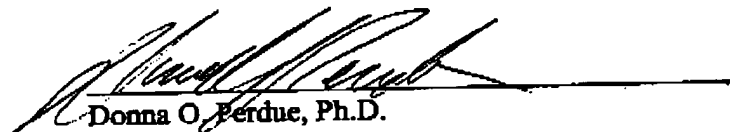
If the Examiner would like to discuss any of the issues raised in the Office Action, Applicant's representative can be reached at (858) 509-4093.

Please charge any additional fees, or make any credits, to Deposit Account No. 03-3975.

Respectfully submitted,

Date:

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